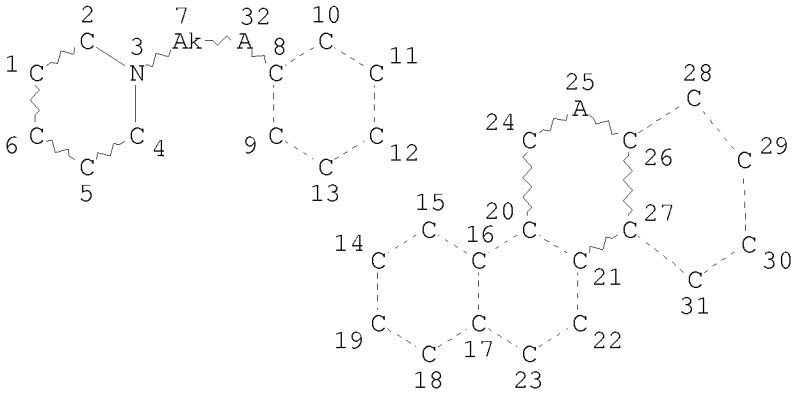
=> d l1
L1 HAS NO ANSWERS
L1 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 9 3 31
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

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FULL SEARCH INITIATED 16:38:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 98194 TO ITERATE

100.0% PROCESSED 98194 ITERATIONS 89 ANSWERS
SEARCH TIME: 00.00.01

L3 89 SEA SSS FUL L1

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COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	193.08	193.30

FILE 'CAPLUS' ENTERED AT 16:38:40 ON 17 AUG 2009
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FILE COVERS 1907 - 17 Aug 2009 VOL 151 ISS 8
FILE LAST UPDATED: 16 Aug 2009 (20090816/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

The ALL, BIB, MAX, and STD display formats in the CA/CAplus family of databases have been updated to include new citing references information. This enhancement may impact record import into database management software. For additional information, refer to NEWS 9.

=> s l3
L4   21 L3

=> d bib abs 1-21

L4   ANSWER 1 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN   2008:1007107 CAPLUS
DN   149:315569
TI   Therapeutic release agents, esters of alkylcarbamic acids, as inhibitors of fatty acid amide hydrolase activity
IN   Dasse, Olivier; Parrott, Jeff A.; Putman, David; Adam, Julia
PA   N.V. Organon, Neth.
SO   PCT Int. Appl., 250pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008100977	A2	20080821	WO 2008-US53785	20080213
	WO 2008100977	A3	20081218		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI	US 2007-889909P	P	20070214		
	US 2007-948082P	P	20070705		

OS   MARPAT 149:315569
AB   Pharmacol. inhibition of fatty acid amide hydrolase (FAAH) activity leads to increased levels of fatty acid amides. Esters of alkylcarbamic acids are disclosed that are inhibitors of FAAH activity. Compds. disclosed herein inhibit FAAH activity. Described herein are processes for the

preparation of esters of alkylcarbamic acid compds., compns. that include them, and methods of use thereof. Thus, to prepare a parenteral pharmaceutical composition for injection, 100 mg of a water-soluble salt of a compound of the invention was dissolved in DMSO and mixed with 10 mL of 0.9% sterile saline; the mixture was incorporated into dosage form unit suitable for administration by injection.

L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:610508 CAPLUS
DN 147:203049
TI Unbiasing Scoring Functions: A New Normalization and Rescoring Strategy
AU Carta, Giorgio; Knox, Andrew J. S.; Lloyd, David G.
CS Molecular Design Group School of Biochemistry Immunology, Trinity College Dublin, Dublin, 2, Ire.
SO Journal of Chemical Information and Modeling (2007), 47(4), 1564-1571
CODEN: JCISD8; ISSN: 1549-9596
PB American Chemical Society
DT Journal
LA English
AB Ligand bias can contribute significantly to the number of false positives observed in a virtual screening campaign. Using a receptor-based docking approach against a well-established target of therapeutic importance, estrogen receptor α (ERα), coupled with several common scoring functions (ChemGuass, ChemGauss2, ChemScore, ScreenScore, ShapeGauss, and PLP), taken both individually and as a consensus, the authors sought to examine the characteristics of mols. retrieved by each. It has been previously shown that scoring functions (mainly empirical) exhibit bias in prioritizing more complicated mols. arising from additive components within the function. Using Spearmen's correlation coefficient, the authors show that a large set of descriptors calculated for a docked set of mols. exhibit pos. correlation with the ranked position in a hit list. Moreover, most of these descriptors correlate well with MW. To this end, rather than penalizing the docked score of all heavy mol. weight (MW) mols. and rewarding those of lower MW, as is common practice, the authors examine the impact of penalizing the score only of those mols. which were of higher MW, leaving lower MW mols. unaffected. Here, the authors introduce a new power function to aid the process. Using scoring frequency anal. and SIFt fingerprints, the authors achieved a more meaningful anal. of virtual screening (VS) performance than with enrichment calcns., facilitating target-specific VS method development.
OSC.G 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:242067 CAPLUS
DN 146:474747
TI Protein Flexibility and Species Specificity in Structure-Based Drug Discovery: Dihydrofolate Reductase as a Test System
AU Bowman, Anna L.; Lerner, Michael G.; Carlson, Heather A.
CS Department of Medicinal Chemistry and Biophysics Research Division, University of Michigan, Ann Arbor, MI, 48109-1065, USA
SO Journal of the American Chemical Society (2007), 129(12), 3634-3640
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB In structure-based drug discovery, researchers would like to identify all possible scaffolds for a given target. However, techniques that push the boundaries of chemical space could lead to many false positives or inhibitors that lack specificity for the target. Is it possible to broadly identify

the appropriate chemical space for the inhibitors and yet maintain target specificity. To address this question, we have turned to dihydrofolate reductase (DHFR), a well-studied metabolic enzyme of pharmacol. relevance. We have extended our multiple protein structure (MPS) method for receptor-based pharmacophore models to use multiple x-ray crystallog. structures. Models were created for DHFR from human and Pneumocystis carinii. These models incorporate a fair degree of protein flexibility and are highly selective for known DHFR inhibitors over drug-like non-inhibitors. Despite sharing a highly conserved active site, the pharmacophore models reflect subtle differences between the human and P. Carinii forms, which identify species-specific, high-affinity inhibitors. We also use structures of DHFR from Candida albicans as a counter example. The available crystal structures show little flexibility, and the resulting models give poorer performance in identifying species-specific inhibitors. Therapeutic success for this system may depend on achieving species specificity between the related human host and these key fungal targets. The MPS technique is a promising advance for structure-based drug discovery for DHFR and other proteins of biomedical interest.

OSC.G 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:408205 CAPLUS
DN 146:870
TI Three-dimensional models of non-steroidal ligands: A comparative molecular field analysis
AU Menezes, Irwin R. A.; Leitao, Andrei; Montanari, Carlos A.
CS Nucleo de Estudos em Quimica Medicinal-NEQUIM, Departamento de Quimica, Universidade Federal de Minas Gerais, Belo Horizonte-MG, 31270-901, Brazil
SO Steroids (2006), 71(6), 417-428
CODEN: STEDAM; ISSN: 0039-128X
PB Elsevier B.V.
DT Journal
LA English
AB The estrogen receptor, ER, is an important biol. target whose inhibition is known to be therapeutically relevant in the treatment of postmenopausal osteoporosis. In the present study, two prediction methods (CoMFA and GRIND (Almond)) were used to describe the binding modes of a set of estrogen receptor ligands. The critical alignment step presented in CoMFA was solved by using the information of the mol. descriptors space generated by grid-independent descriptors (GRIND). Then, it was possible to build robust and high predictive models based on the alignment-independent model. Since the structure of estrogen receptor is solved, the results of the present 3D QSAR models, given by the PLS maps based on mol. interaction fields (MIF) were compared to ligand-binding ER domains and showed good agreement.

OSC.G 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:94509 CAPLUS
DN 144:327327
TI Knowledge-Based Interaction Fingerprint Scoring: A Simple Method for Improving the Effectiveness of Fast Scoring Functions
AU Mpamhanga, Chidochangu P.; Chen, Beining; McLay, Iain M.; Willett, Peter
CS Department of Chemistry, University of Sheffield, Sheffield, S3 7HF, UK
SO Journal of Chemical Information and Modeling (2006), 46(2), 686-698
CODEN: JCISD8; ISSN: 1549-9596
PB American Chemical Society

DT Journal
LA English
AB A new method for the postprocessing of docking outputs has been developed, based on encoding putative 3D binding modes (docking solns.) as ligand-protein interactions into simple bit strings, a method analogous to the structural interaction fingerprint. Instead of employing traditional scoring functions, the method uses a series of new, knowledge-based scores derived from the similarity of the bit strings for each docking solution to that of a known reference binding mode. A GOLD docking study was carried out using the Bissantz estrogen receptor antagonist set along with the new scoring method. Superior recovery rates, with up to 2-fold enrichments, were observed when the new knowledge-based scoring was compared to the GOLD fitness score. In addition, top ranking sets of mols. (actives and potential actives or decoys) were structurally diverse with low mol. wts. and structural complexities. Principal component anal. and clustering of the fingerprints permits the easy separation of active from inactive binding modes and the visualization of diverse binding modes.
OSC.G 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:26815 CAPLUS
DN 144:163512
TI A Selective Estrogen Receptor Modulator for the Treatment of Hot Flushes
AU Wallace, Owen B.; Lauwers, Kenneth S.; Dodge, Jeffrey A.; May, Scott A.; Calvin, Joel R.; Hinklin, Ronald; Bryant, Henry U.; Shetler, Pamela K.; Adrian, Mary D.; Geiser, Andrew G.; Sato, Masahiko; Burris, Thomas P.
CS Lilly Research Laboratories, Lilly Corporate Center, Eli Lilly and Company, Indianapolis, IN, 46285, USA
SO Journal of Medicinal Chemistry (2006), 49(3), 843-846
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 144:163512
AB A selective estrogen receptor modulator (SERM) for the potential treatment of hot flushes is described. (R)-(+)-7,9-difluoro-5-[4-(2-piperidin-1-ylethoxy)phenyl]-5H-6-oxachrysen-2-ol, LSN2120310, potently binds ERα and ERβ and is an antagonist in MCF-7 breast adenocarcinoma and Ishikawa uterine cancer cell lines. The compound is a potent estrogen antagonist in the rat uterus. In ovariectomized rats, the compound lowers cholesterol, maintains bone mineral d., and is efficacious in a morphine dependent rat model of hot flush efficacy.
OSC.G 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:23807 CAPLUS
DN 144:343802
TI Probing the binding of ligands to estrogen receptor using an empirical system
AU Dottorini, T.; Cozzini, P.
CS Department of Experimental Medicine and Biochemical Sciences, Microbiology Section, University of Perugia, Perugia, 06122, Italy
SO International Journal of Quantum Chemistry (2005), Volume Date 2006, 106(3), 641-646
CODEN: IJQCB2; ISSN: 0020-7608
PB John Wiley & Sons, Inc.
DT Journal

LA English

AB The estrogen receptor (ER) is a ligand-regulated transcription factor whose activity as an inducer or repressor of gene transcription depends on the nature of the ligand to which it is bound. The aim of this work is to evaluate the behavior of a set of compds. (antagonist mols.), using different docking expts., to understand the relationship between ERα and such new ligands. With regard to the chemical properties of the ligands analyzed, the authors defined a specific guideline procedure designed for docking expts. In the authors' approach, the authors propose the use of the HINT scoring function in docking methodologies as a means of assessing the consistency of a docking solution, to discriminate correctly or near-correctly docked orientations from incorrectly docked ones, thus compensating for the lack of exptl. data.

OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:732663 CAPLUS

DN 143:193907

TI Preparation of 5H-6-oxa-chrysene derivatives as selective estrogen receptor modulators

IN Dodge, Jeffrey Alan; Hopkins, Randall Bruce; Wallace, Owen Brendan

PA Eli Lilly and Company, USA

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

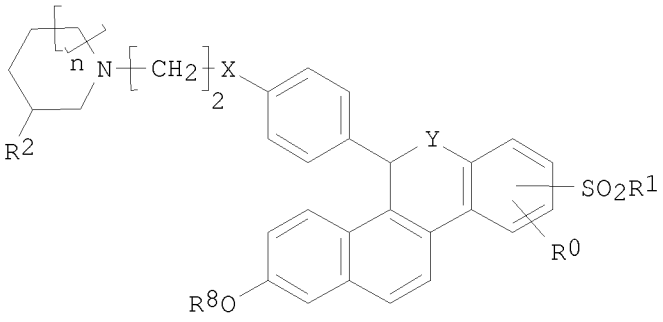
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005073244	A1	20050811	WO 2005-US19	20050118
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1713820	A1	20061025	EP 2005-704873	20050118
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	US 20080221163	A1	20080911	US 2006-597090	20060711
PRAI	US 2004-538302P	P	20040122		
	WO 2005-US19	W	20050118		

OS CASREACT 143:193907; MARPAT 143:193907

GI



I

AB The present invention relates to a selective estrogen receptor modulators, I (n = independently 0,1,2; R8 = H, SO2-alkyl, COR3; R0 = OH, CF3, C1-6 alkyl, or C1-6 alkoxy; R1 = C1-6 alkyl, C1-6 alkoxy, amine CF3, CH2CF3; R2 = H, Me; X = O or substituted amine; Y = O or S), for treating endometriosis and uterine leiomyoma.

OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:732631 CAPLUS

DN 143:193912

TI Preparation of piperidine derivatives as estrogen antagonists in the uterus that do not stimulate the ovaries for treating endometriosis and uterine leiomyoma

IN Dally, Robert Dean; Dodge, Jeffrey Alan; Hummel, Conrad Wilson; Jones, Scott Alan; Shepherd, Timothy Alan; Wallace, Owen Brendan; Weber, Wayne Woodrow, II

PA Eli Lilly and Company, USA

SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005073205	A1	20050811	WO 2005-US21	20050118
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1709022	A1	20061011	EP 2005-704875	20050118
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	US 20070111988	A1	20070517	US 2006-597008	20060706
PRAI	US 2004-538441P	P	20040122		
	US 2004-582945P	P	20040625		
	WO 2005-US21	W	20050118		

OS CASREACT 143:193912; MARPAT 143:193912

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to alcs. (shown as I; variables defined below; e.g. [4-[6-methoxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]phenyl]methanol) or a pharmaceutical acid addition salt thereof and carboxy compds. (shown as II; variables defined below; e.g. 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]-N,N-dimethylbenzamide hydrochloride) or a pharmaceutical salt thereof as selective estrogen receptor modulators, useful, e.g., for treating endometriosis and/or uterine leiomyoma/leiomyomata. Other similar Markush formulas for claimed compds. are given in the claims. In the Ishikawa cell proliferation assay, cell proliferation (using an alkaline phosphatase readout) was measured in both an agonist mode in the presence of I or II alone, and in an antagonist mode in which the ability of I or II to block estradiol stimulation of growth was measured. In the agonist mode, the compds. of 14 examples were tested and are less stimulatory than tamoxifen. For example, 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]-N,N-dimethylbenzamide hydrochloride had a relative % efficacy of 15% and 2-hydroxy-5-[4-[2-(piperidin-1-yl)ethoxy]phenyl]-5H-6-oxachrysene-7-carboxylic acid trifluoroacetate had a relative % efficacy of 25%. In the antagonist mode, these same compds. inhibited greater than at least 80% of the 1 nM estradiol response. For example, 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]-N,N-dimethylbenzamide hydrochloride had an IC50 of 9 nM and a % efficacy of 95% and 2-hydroxy-5-[4-[2-(piperidin-1-yl)ethoxy]phenyl]-5H-6-oxachrysene-7-carboxylic acid trifluoroacetate had an IC50 of 36 nM and a % efficacy of 92%. Results of a 3-day rat uterus antagonist assay are also reported. One example compound was tested in a 4-day OVX rat uterine agonist assay and did not cause any dose-related statistically significant increase in uterine eosinophil peroxidase activity. Two example compds. did not significantly elevate circulating estradiol or LH levels. For I: m = 0-2; R0 is H, F or OH; R1 is H, SO2(n-C4-C6 alkyl) or COR4; R2 is H or Me provided that if m is 1 or 2, then R2 must be H and that if m is 0, then R2 must be Me; X is O or NR5; Y is S or CH:CH; R4 is C1-C6 alkyl, C1-C6 alkoxy, NR6R7, phenoxy, or Ph (un)substituted with halo; R5 is H or C1-C6 alkyl; R6 and R7 = H, C1-C6 alkyl or phenyl; R is H and X1 is O, CH2 or CO or R combines with X1 to form III (X2 is O or S); and R3 and R3a = H or C1-C6 alkyl. For II: m = 0-2; R1 is H, SO2(n-C4-C6 alkyl) or COR4; R2 is H or Me provided that if m is 1 or 2, then R2 must be H and that if m is 0, then R2 must be Me; X is O or NR5; Y is S or CH:CH; R4 is C1-C6 alkyl, C1-C6 alkoxy, NR6R7, phenoxy, or Ph (un)substituted with halo; R5 is H or C1-C6 alkyl; R6 and R7 = H, C1-C6 alkyl or phenyl; R is H and X1 is O, CH2 or CO or R combines with X1 to form IV (X2 is O or S); R3b is NR8R9 or OR10 or when R is H, R3b may combine with the Ph with which it is attached to form V (W and W1 are CH2 or C:O provided that at least one of W or W1 must be C:O; X3 is NR11 or O; R8 and R9 = H or C1-C6 alkyl or R8 and R9 may combine with the N to which they are both attached to form a morpholino, pyrrolidino or piperidino ring; R10 and R11 = H or C1-C6 alkyl). Although the methods of preparation are not claimed, .apprx.70 example prepns. are included. For example, 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]benzamide hydrochloride was prepared (88 %) by HCl treatment of 3-[6-hydroxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl]benzonitrile hydrochloride, which was prepared (98 %) by coupling trifluoromethanesulfonic acid 6-methoxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl ester (preparation described) with

3-cyanophenylboronic acid followed by conversion of the OMe to OH group.
OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:732630 CAPLUS
DN 143:211842
TI Preparation of piperidine derivatives as selective estrogen receptor modulators for the treatment of vasomotor symptoms
IN Dally, Robert Dean; Dodge, Jeffrey Alan; Frank, Scott Alan; Hinklin, Ronald Jay; Shepherd, Timothy Alan; Wallace, Owen Brendan
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005073204	A1	20050811	WO 2005-US20	20050118
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005207821	A1	20050811	AU 2005-207821	20050118
	CA 2551956	A1	20050811	CA 2005-2551956	20050118
	EP 1709021	A1	20061011	EP 2005-704874	20050118
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
	CN 1910167	A	20070207	CN 2005-80002914	20050118
	BR 2005006721	A	20070502	BR 2005-6721	20050118
	JP 2007519721	T	20070719	JP 2006-551097	20050118
	SG 149867	A1	20090227	SG 2009-414	20050118
	ZA 2006005665	A	20080528	ZA 2006-5665	20060710
	US 20090023917	A1	20090122	US 2006-597241	20060718
	KR 2006129277	A	20061215	KR 2006-714630	20060720
	KR 849559	B1	20080731		
	MX 2006008291	A	20061002	MX 2006-8291	20060721
	NO 2006003760	A	20061016	NO 2006-3760	20060822
	IN 2006KN02478	A	20070615	IN 2006-KN2478	20060822
	KR 2008016755	A	20080221	KR 2008-703065	20080205
PRAI	US 2004-538342P	P	20040122		
	US 2004-538442P	P	20040122		
	WO 2005-US20	W	20050118		
	KR 2006-714630	A3	20060720		

OS CASREACT 143:211842; MARPAT 143:211842
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to selective estrogen receptor modulators (no data; shown as I; variables defined below; e.g. 1-[2-[4-[[2-(2,6-difluorophenyl)-6-methoxynaphthalen-1-yl]oxy]phenoxy]ethyl]piperidine (shown as II)) or pharmaceutical acid addition salts thereof useful for treating vasomotor symptoms, in particular hot flashes, night sweats and other symptoms that affect women around menopause. In a morphine withdrawal, rat hot flash model, representative I were tested ≤30 mg/kg PO and caused an attenuation of tail skin temperature increase, as measured by temperature change 15 min post naloxone injection or AUC over 45 min post naloxone administration. For I: m = 0-2; n = 1-4; R is H or Me provided that if m is 1 or 2, then R must be H and that if m is 0, then R must be Me; R1 is H, SO2(n-C4-C6 alkyl) or COR2; X is O or NR3; X1 is O, CH2 or C:O; R6 is H or F or R6 combines with X1 to form III (Y is O, S, SO or NR4; e.g. 7,9-difluoro-5-[4-[2-(piperidin-1-yl)ethoxy]phenyl]-5H-6-oxachrysen-2-ol (shown as IV)); R2 is C1-C6 alkyl, C1-C6 alkoxy, NR5R5a, phenoxy, or Ph (un)substituted with halo; R3 and R4 = H or C1-C6 alkyl; and R5 and R5a = H, C1-C6 alkyl or Ph. Although the methods of preparation are not claimed, .apprx.150 example prepns. are included. For example, II was prepared (32 %) from trifluoromethanesulfonic acid 6-methoxy-1-[4-[2-(piperidin-1-yl)ethoxy]phenoxy]naphthalen-2-yl ester (preparation given) and (2,6-difluorophenyl)boronic acid in DMF using potassium phosphate and tetrakis(triphenylphosphine)palladium(0).
OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:478998 CAPLUS
DN 143:165982
TI A pharmacophore-based evolutionary approach for screening selective estrogen receptor modulators
AU Yang, Jinn-Moon; Shen, Tsai-Wei
CS Department of Biological Science and Technology, National Chiao Tung University, Hsinchu, Taiwan
SO Proteins: Structure, Function, and Bioinformatics (2005), 59(2), 205-220
CODEN: PSFBAF
PB Wiley-Liss, Inc.
DT Journal
LA English
AB The authors developed a pharmacophore-based evolutionary approach for virtual screening. This tool, termed the Generic Evolutionary Method for mol. DOCKing (GEMDOCK), combines an evolutionary approach with a new pharmacophore-based scoring function. The former integrates discrete and continuous global search strategies with local search strategies to expedite convergence. The latter, integrating an empirical-based energy function and pharmacol. preferences (binding-site pharmacol. interactions and ligand preferences), simultaneously serves as the scoring function for both mol. docking and postdocking analyses to improve screening accuracy. The authors apply pharmacol. interaction preferences to select the ligands that form pharmacol. interactions with target proteins, and use the ligand preferences to eliminate the ligands that violate the electrostatic or hydrophilic constraints. The authors assessed the accuracy of our approach using human estrogen receptor (ER) and a ligand database from the comparative studies of Bissantz et al. (J Med Chem 2000;43:4759-4767). Using GEMDOCK, the average goodness-of-hit (GH) score was 0.83 and the average false-pos. rate was 0.13% for ER antagonists, and the average GH score was 0.48 and the average false-pos. rate was 0.75% for ER agonists. The performance of GEMDOCK was superior to competing methods such as GOLD and DOCK. The authors found that our pharmacophore-based scoring function

indeed was able to reduce the number of false positives; moreover, the resulting pharmacol. interactions at the binding site, as well as ligand preferences, were important to the screening accuracy of our expts. These results suggest that GEMDOCK constitutes a robust tool for virtual database screening.
OSC.G 27 THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (28 CITINGS)
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:548950 CAPLUS
DN 141:134250
TI Is it possible docking and scoring new ligands with few experimental data? Preliminary results on estrogen receptor as a case study
AU Cozzini, P.; Dottorini, T.
CS Molecular Modelling Laboratory, Department of General and Inorganic Chemistry, Parco Area delle Scienze, University of Parma, Parma, 43100, Italy
SO European Journal of Medicinal Chemistry (2004), 39(7), 601-609
CODEN: EJMCA5; ISSN: 0223-5234
PB Elsevier Science Ltd.
DT Journal
LA English
AB Estrogens are steroid hormones playing critical roles in several physiol. processes, which bind the estrogen receptors ERα and ERβ. Aim of this work is to analyze, by different docking expts., the behavior of a set of compds., mimicking estrogens activity, to understand the relationship between ERα and such new ligands. Main goal is to verify, using a widely tested scoring software procedure applied on a set of 10 compds., the possibility to produce new lead candidate mols. in lack of, or with few exptl. data. The authors' preliminary results reveal the significance of HINT software as a scoring function in docking methodol. and specifically, as a mean for assessing the consistency of docking solns.
OSC.G 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:42543 CAPLUS
DN 140:246121
TI Ligand-Based Structural Hypotheses for Virtual Screening
AU Jain, Ajay N.
CS UCSF Cancer Research Institute and Comprehensive Cancer Center, University of California, San Francisco, CA, 94143-0128, USA
SO Journal of Medicinal Chemistry (2004), 47(4), 947-961
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB The majority of drug targets for small mol. therapeutics are proteins whose three-dimensional structure is not known to sufficient resolution to permit structure-based design. All three-dimensional QSAR approaches have a requirement for some hypothesis of ligand conformation and alignment, and predictions of mol. activity critically depend on this ligand-based binding site hypothesis. The mol. similarity function used in the Surflex docking system, coupled with quant. pressure to minimize overall mol. volume, forms an effective objective function for generating hypotheses of bioactive conformations of sets of small mols. binding to their cognate proteins. Results are presented, assessing utility of the method for ligands of the serotonin, histamine, muscarinic, and GABAA receptors. The

Surflex similarity module (Surflex-Sim) was able, in each case, to distinguish true ligands from random compds. using models constructed from just two or three known ligands. True pos. rates of 60% were achieved with false pos. rates of 0-3%; the theor. enrichment rates were over 150-fold compared with random screening. The methods are practically applicable for rational design of ligands and for high-throughput virtual screening and offer competitive performance to many structure-based docking algorithms.

OSC.G 38 THERE ARE 38 CAPLUS RECORDS THAT CITE THIS RECORD (38 CITINGS)
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2003:678670 CAPLUS
DN 139:192008
TI Methods and composition for treating decreased libido in women with estrogenic components
IN Coelingh Bennink, Herman Jian Tijmen
PA Pantarhei Bioscience B.V., Neth.
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003070253	A1	20030828	WO 2003-NL125	20030219
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003206442	A1	20030909	AU 2003-206442	20030219
PRAI	EP 2002-75696	A	20020221		
	WO 2003-NL125	W	20030219		

AB The present invention is concerned with a method of treating decreased libido in pre-menopausal women, said decreased libido being the result of the repeated administration of a progestogenic component, wherein the method comprises the administration of the estrogenic component to a woman in an effective amount to improve the woman's libido. The present method is particularly suited for treating decreased libido in women using hormonal contraceptives that employ administration of a progestogenic component.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2003:498000 CAPLUS
DN 139:176251
TI BHB: A simple knowledge-based scoring function to improve the efficiency of database screening
AU Feher, Miklos; Deretey, Eugen; Roy, Samir
CS SignalGene Inc., Guelph, ON, N1G 4P7, Can.
SO Journal of Chemical Information and Computer Sciences (2003), 43(4), 1316-1327
CODEN: JCISD8; ISSN: 0095-2338
PB American Chemical Society

DT Journal
LA English
AB A new knowledge-based scoring function was developed in this work to facilitate the rapid ranking of ligands in databases. The acronym of the method is BHB based on the descriptors it utilizes:buriedness, hydrogen bonding, and binding energy. Receptor buriedness is a measure of how well mols. occupy the binding pocket in comparison to known high-affinity ligands or, alternatively, whether they have contact with identified residues in the pocket. The possibility of hydrogen bond formation is checked for selected residues that are recognized as being important in the binding of known ligands. The approx. binding energy is calculated from the thermodn. cycle using the optimized bound and free solvent conformations of the ligand-receptor system. The information necessary for the scoring function can ideally be gleaned from the 3D structure of the receptor-ligand complex. Alternatively, the descriptors can be derived from the 3D structure of the unbound receptor, provided this receptor has a known ligand that binds to the given site with nanomolar activity. We show that the new scoring functions provide up to 12 times improvement in enrichment compared to the popular com. docking program GOLD.
OSC.G 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:940242 CAPLUS
DN 137:380017
TI Estrogen receptor β-based hypertension treatment and assay
IN Gustafsson, Jan-Ake; Bian, Zhao
PA Karo Bio AB, Swed.
SO Brit. UK Pat. Appl., 28 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2374412	A	20021016	GB 2001-9091	20010411
PRAI GB 2001-9091		20010411		

AB Methods are disclosed for assaying compds. for blood pressure-modulating activity. The methods include determining the ability of the compound to affect estrogen receptor β (ERβ) activity. The invention also discloses the use of ERβ-modulating compds. for modulating blood pressure, in particular for treating hypertension.
OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:210373 CAPLUS
DN 137:87830
TI Molecular simulation of interaction between estrogen receptor and selective estrogen receptor modulators
AU Guo, Zong-Ru; Yi, Xiang; Xu, Zhi-Bin
CS Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100050, Peop. Rep. China
SO Acta Pharmacologica Sinica (2002), 23(3), 208-212
CODEN: APSCG5; ISSN: 1671-4083
PB Science Press
DT Journal
LA English
AB Aim: To study the mechanism of interaction between a series of potent racemic selective estrogen receptor modulators (SERM) and estrogen

receptors (ER). Methods: Active conformations of these conformationally restricted raloxifene analogs in binding pocket were determined by mol. mechanics. The interactive energies between ligand and receptor were calculated by docking program. Results: Both R and S configurations of these SERM were accommodated by the binding pocket of ER. The hydroxy group of compds. forms hydrogen bonds with amino acid residues of ER and the phenolic group mimics the A-ring of estradiol. The most potential compds. were those with two hydroxy groups and accommodated by binding pocket in S configuration with phenolic group at C(16) imitating A-ring of estradiol. Conclusion: Chiral center conferred little effect on the binding affinity of these conformationally restricted raloxifene analogs. The hydroxy group(s) play(s) a critical role to the orientation of compds. in active pocket of ER and the binding between ligand and receptor.

OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2000:818588 CAPLUS
DN 134:125545
TI Protein-Based Virtual Screening of Chemical Databases. 1. Evaluation of Different Docking/Scoring Combinations
AU Bissantz, Caterina; Folkers, Gerd; Rognan, Didier
CS Department of Applied Biosciences, ETH Zuerich, Zurich, CH-8057, Switz.
SO Journal of Medicinal Chemistry (2000), 43(25), 4759-4767
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Three different database docking programs (Dock, FlexX, Gold) have been used in combination with seven scoring functions (Chemscore, Dock, FlexX, Fresno, Gold, Pmf, Score) to assess the accuracy of virtual screening methods against two protein targets (thymidine kinase, estrogen receptor) of known three-dimensional structure. For both targets, it was generally possible to discriminate about 7 out of 10 true hits from a random database of 990 ligands. The use of consensus lists common to two or three scoring functions clearly enhances hit rates among the top 5% scorers from 10% (single scoring) to 25-40% (double scoring) and up to 65-70% (triple scoring). However, in all tested cases, no clear relationships could be found between docking and ranking accuracies. Moreover, predicting the absolute binding free energy of true hits was not possible whatever docking accuracy was achieved and scoring function used. As the best docking/consensus scoring combination varies with the selected target and the physicochem. of target-ligand interactions, we propose a two-step protocol for screening large databases: (i) screening of a reduced dataset containing a few known ligands for deriving the optimal docking/consensus scoring scheme, (ii) applying the latter parameters to the screening of the entire database.

OSC.G 383 THERE ARE 383 CAPLUS RECORDS THAT CITE THIS RECORD (384 CITINGS)
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1998:215077 CAPLUS
DN 128:266187
OREF 128:52547a,52550a
TI Synthesis and Pharmacology of Conformationally Restricted Raloxifene Analogs: Highly Potent Selective Estrogen Receptor Modulators
AU Grese, Timothy A.; Pennington, Lewis D.; Sluka, James P.; Adrian, M. Dee; Cole, Harlan W.; Fuson, Tina R.; Magee, David E.; Phillips, D. Lynn; Rowley, Ellen R.; Shetler, Pamela K.; Short, Lorri L.; Venugopalan,

Murali; Yang, Na N.; Sato, Masahiko; Glasebrook, Andrew L.; Bryant, Henry U.

CS Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA

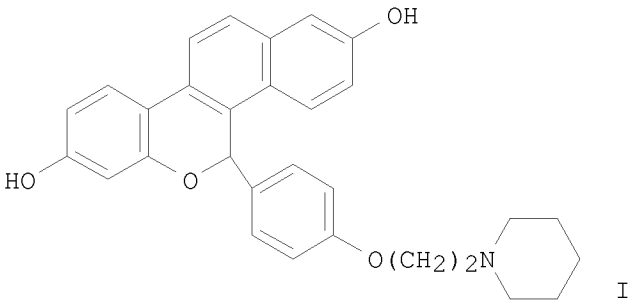
SO Journal of Medicinal Chemistry (1998), 41(8), 1272-1283
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

GI



I

AB Raloxifene is a selective estrogen receptor modulator (SERM) which is currently under clin. evaluation for the prevention and treatment of postmenopausal osteoporosis. In vivo structure-activity relationships and mol. modeling studies indicated that the orientation of the basic amine-containing side chain of raloxifene relative to the stilbene plane is an important discriminating factor for the maintenance of tissue selectivity. A series of raloxifene analogs where this side chain is held in an orientation which is orthogonal to the stilbene plane, similar to the low-energy conformation predicted for raloxifene were constructed. These analogs were prepared and tested for their activity in a series of in vitro and in vivo biol. assays reflective of the SERM profile. The ability of these analogs to (1) bind the estrogen receptor, (2) antagonize estrogen-stimulated proliferation of MCF-7 cells in vitro, (3) stimulate TGF-β3 gene expression in cell culture, (4) inhibit the uterine effects of ethynyl estradiol in immature rats, and (5) potently reduce serum cholesterol and protect against osteopenia in ovariectomized (OVX) rats without estrogen-like stimulation of uterine tissue is detailed. These data demonstrate that LY357489 (I) is among the most potent SERMs described to date with in vivo efficacy on bone and cholesterol metabolism in OVX rats at doses as low as 0.01 mg/kg/d.

OSC.G 92 THERE ARE 92 CAPLUS RECORDS THAT CITE THIS RECORD (92 CITINGS)

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1998:180547 CAPLUS

DN 128:217362

OREF 128:43059a,43062a

TI Preparation of benzothienobenzopyrans, benzophenanthridines, and related compounds for treatment of postmenopausal syndrome.

IN Grese, Timothy Alan

PA Eli Lilly and Co., USA

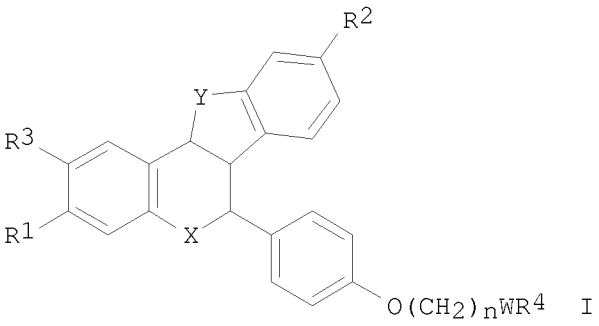
SO U.S., 39 pp.
CODEN: USXXAM

DT Patent

LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5726186	A	19980310	US 1996-696279	19960813
	US 6004971	A	19991221	US 1997-878799	19970619
	US 6133288	A	20001017	US 1999-436743	19991109
PRAI	US 1995-3496P	P	19950908		
	US 1996-696279	A3	19960813		
	US 1997-878799	A1	19970619		

OS MARPAT 128:217362
GI



I

AB Title compds. [I; X = O, S; Y = O, S, CH2, CH2CH2, CH:CH, NR5; R1-R3 = H, OH, alkoxy, PhCO2, alkylcarbonyloxy, alkylsulfonyloxy, OSO2CF3, Cl, F; n = 1, 2; W = CH2, CO; R4 = 1-piperidinyl, 2-oxo-1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 2-oxo-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, 1-hexamethyleneimino; R5 = alkyl, PhCO, alkylcarbonyl, phenoxycarbonyl, alkoxycarbonyl, alkylsulfonyl, phenylsulfonyl, SO2CF3], were prepared Thus, 6-methoxythianaphthalen-2-one (preparation given) was stirred with 4-methoxysalicylaldehyde and Et3N in CH2Cl2 to give 6a,11a-dihydro-3,9-dimethoxy-6H-[1]benzothieno[3,2-c][1]benzopyran-6-one. This was converted in several steps to 3,9-dihydroxy-6-[4-[2-(1-piperidinyl)ethoxy]phenyl]-6H-[1]benzothieno[3,2-c][1]benzopyran. The latter at 0.1 mg/kg in ovariectomized rats reduced serum cholesterol by 72.8%.

OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1997:286346 CAPLUS
DN 126:264018
OREF 126:51137a,51140a
TI Preparation of pentacyclic compounds for the treatment conditions associated with post-menopausal syndrome
IN Grese, Timothy Alan
PA Eli Lilly and Co., USA
SO Eur. Pat. Appl., 72 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 761669	A2	19970312	EP 1996-306351	19960902
	EP 761669	A3	19971029		
	EP 761669	B1	20001122		
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA 2230974	A1	19970313	CA 1996-2230974	19960826
	WO 9709044	A1	19970313	WO 1996-US13778	19960826
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
	RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9669590	A	19970327	AU 1996-69590	19960826
	AU 705454	B2	19990520		
	CN 1201392	A	19981209	CN 1996-198083	19960826
	HU 9802213	A2	19990201	HU 1998-2213	19960826
	HU 9802213	A3	20000328		
	BR 9610356	A	19990706	BR 1996-10356	19960826
	JP 11514347	T	19991207	JP 1997-511257	19960826
	JP 3688299	B2	20050824		
	CZ 286236	B6	20000216	CZ 1998-678	19960826
	IL 123560	A	20020210	IL 1996-123560	19960826
	IL 140162	A	20020210	IL 1996-140162	19960826
	AT 197712	T	20001215	AT 1996-306351	19960902
	NO 9800936	A	19980507	NO 1998-936	19980304
	GR 3035253	T3	20010430	GR 2001-400073	20010117
PRAI	US 1995-3496P	P	19950908		
	IL 1996-123560	A3	19960826		
	WO 1996-US13778	W	19960826		

OS MARPAT 126:264018

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I and II; X = O, S, NR5 (wherein R5 = C1-3 alkyl, COPh, SO2CF3, etc.); Y = O, S, CH2, CH2CH2, CH:CH, NR5; B = CH2, CO; R1-R3 = H, OH, O(C1-C4 alkyl), etc.; n = 1, 2; W = CH2, CO; R4 = 1-piperidinyl, 2-oxo-1-piperidinyl, 1-pyrrolidinyl, etc.], useful for the treatment of the various conditions associated with post-menopausal syndrome such as osteoporosis, and uterine fibroid disease, endometriosis, and aortal smooth muscle cell proliferation, and as bone loss or resorption inhibitors and serum cholesterol levels lowering agents, were prepared and formulated. Thus, reaction of 3,9-bis[(tert-butyldimethylsilyl)oxy]-6-phenox-6-H-[1]benzothieno[3,2-c][1]benzopyran with 4-(2-piperidinoethoxy)phenylmagnesium bromide in PhMe/THF followed by removal of TBDMS groups with TBAF in THF afforded III which showed IC50 of 0.2 nM against MCF-7 breast adenocarcinoma cells proliferation.

OSC.G 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)